Met Asp Trp Pro His Asn Leu Leu Phe Leu Leu Thr Ile Ser Ile
1 5 10 15

Phe Leu Gly Leu Gly Gln Pro Arg Ser Pro Lys Ser Lys Arg Lys
20 25 30

Gly Gln Gly Arg Pro Gly Pro Leu Ala Pro Gly Pro His Gln Val
35 40 45

Pro Leu Asp Leu Val Ser Arg Met Lys Pro Tyr Ala Arg Met Glu
50 55 60

Glu Tyr Glu Arg Asn Ile Glu Glu Met Val Ala Gln Leu Arg Asn
65 70 75

Ser Ser Glu Leu Ala Gln Arg Lys Cys Glu Val Asn Leu Gln Leu
80 85 90

Trp Met Ser Asn Lys Arg Ser Leu Ser Pro Trp Gly Tyr Ser Ile
95 100 105

Asn His Asp Pro Ser Arg Ile Pro Val Asp Leu Pro Glu Ala Arg
110 115 120

Cys Leu Cys Leu Gly Cys Val Asn Pro Phe Thr Met Gln Glu Asp
125 130 135

Arg Ser Met Val Ser Val Pro Val Phe Ser Gln Val Pro Val Arg
140 145 150

Arg Arg Leu Cys Pro Pro Pro Pro Arg Thr Gly Pro Cys Arg Gln
155 160 165

Arg Ala Val Met Glu Thr Ile Ala Val Gly Cys Thr Cys Ile Phe
170 175 180

FIGURE 1

aggcgggcag cagctgcagg ctgaccttgc agcttggcgg aatggactgg 50

cctcacaacc tgctgtttct tcttaccatt tccatcttcc tggggctggg 100

ccagcccagg agccccaaaa gcaagaggaa ggggcaaggg cggcctgggc 150

ccctggcccc tggccctcac caggtgccac tggacctggt gtcacggatg 200

aaaccgtatg cccgcatgga ggagtatgag aggaacatcg aggagatggt 250

ggcccagctg aggaacagct cagagctggc ccagagaaag tgtgaggtca 300

acttgcagct gtggatgtcc aacaagagga gcctgtctcc ctggggctac 350

agcatcaacc acgaccccag ccgtatcccc gtggacctgc cggaggcacg 400

gtgcctgtgt ctgggctgtg tgaacccctt caccatgcag gaggaccgca 450

gcatggtgag cgtgccggtg ttcagccagg ttcctgtgcg ccgccgcctc 500

tgcccgccac cgccccgcac agggccttgc cgccagcgcg cagtcatgga 550

gaccatcgct gtgggctgca cctgcatctt ctgaatcacc tggcccagaa 600

gccaggccag cagcccgaga ccatcctcct tgcacctttg tgccaagaaa 650

ggcctatgaa aagtaaacac tgacttttga aagcaag 687

FIGURE 2

```
Met Thr Leu Leu Pro Gly Leu Leu Phe Leu Thr Trp Leu His Thr
  1               5                  10                  15

Cys Leu Ala His His Asp Pro Ser Leu Arg Gly His Pro His Ser
            20                  25                  30

His Gly Thr Pro His Cys Tyr Ser Ala Glu Glu Leu Pro Leu Gly
            35                  40                  45

Gln Ala Pro Pro His Leu Leu Ala Arg Gly Ala Lys Trp Gly Gln
            50                  55                  60

Ala Leu Pro Val Ala Leu Val Ser Ser Leu Glu Ala Ala Ser His
            65                  70                  75

Arg Gly Arg His Glu Arg Pro Ser Ala Thr Thr Gln Cys Pro Val
            80                  85                  90

Leu Arg Pro Glu Glu Val Leu Glu Ala Asp Thr His Gln Arg Ser
            95                 100                 105

Ile Ser Pro Trp Arg Tyr Arg Val Asp Thr Asp Glu Asp Arg Tyr
           110                 115                 120

Pro Gln Lys Leu Ala Phe Ala Glu Cys Leu Cys Arg Gly Cys Ile
           125                 130                 135

Asp Ala Arg Thr Gly Arg Glu Thr Ala Ala Leu Asn Ser Val Arg
           140                 145                 150

Leu Leu Gln Ser Leu Leu Val Leu Arg Arg Arg Pro Cys Ser Arg
           155                 160                 165

Asp Gly Ser Gly Leu Pro Thr Pro Gly Ala Phe Ala Phe His Thr
           170                 175                 180

Glu Phe Ile His Val Pro Val Gly Cys Thr Cys Val Leu Pro Arg
           185                 190                 195

Ser Val
    197
```

FIGURE 3

gccaggtgtg caggccgctc caagcccagc ctgccccgct gccgccacca 50

tgacgctcct ccccggcctc ctgtttctga cctggctgca cacatgcctg 100

gcccaccatg acccctccct caggggggcac ccccacagtc acggtacccc 150

acactgctac tcggctgagg aactgccccct cggccaggcc cccccacacc 200

tgctggctcg aggtgccaag tgggggcagg ctttgcctgt agccctggtg 250

tccagcctgg aggcagcaag ccacaggggg aggcacgaga ggccctcagc 300

tacgacccag tgcccggtgc tgcggccgga ggaggtgttg gaggcagaca 350

cccaccagcg ctccatctca ccctggagat accgtgtgga cacggatgag 400

gaccgctatc cacagaagct ggccttcgcc gagtgcctgt gcagaggctg 450

tatcgatgca cggacgggcc gcgagacagc tgcgctcaac tccgtgcggc 500

tgctccagag cctgctggtg ctgcgccgcc ggccctgctc ccgcgacggc 550

tcggggctcc ccacacctgg ggcctttgcc ttccacaccg agttcatcca 600

cgtccccgtc ggctgcacct gcgtgctgcc ccgttcagtg tgaccgccga 650

ggccgtgggg cccctagact ggacacgtgt gctccccaga gggcaccccc 700

tatttatgtg tatttattgt tatttatatg cctccccccaa cactaccctt 750

ggggtctggg cattccccgt gtctggagga cagcccccca ctgttctcct 800

catctccagc ctcagtagtt gggggtagaa ggagctcagc acctcttcca 850

gcccttaaag ctgcagaaaa ggtgtcacac ggctgcctgt accttggctc 900

cctgtcctgc tcccggcttc ccttacccta tcactggcct caggccccgc 950

aggctgcctc ttcccaacct ccttggaagt acccctgttt cttaaacaat 1000

tatttaagtg tacgtgtatt attaaactga tgaacacatc cccaaaa 1047

FIGURE 4

ggcagcaggg accaagagag gcacgcttgc ccttttatga catcagagct 50

cctggttctt gctccttggg actctgggac ttacaccagt ggcacccctg 100

gctcnnnnnn nnnnnaattc ggtacgaggc tggggttcag gcgggcagca 150

gctgcaggct gaccttgcag cttggcggaa tggactggcc tcacaacctg 200

ctgtttcttc ttaccatttc catcttcctg gggctgggcc agcccaggag 250

ccccaaaagc aagaggaagg ggcaagggcg gcctgggccc ctggtccctg 300

gccctcacca ggtgccactg gacctggtgt cacggatgaa accgtatgcc 350

cgcatggagg agtatgagag gaacatcgag gagatgttgg cccagctgag 400

gaacagttca gagctggccc agagaaagtg tgaggtcaac ttgcagctgt 450

ggatgtccaa caagaggagc ctgtctccct ggggctacag catcaaccac 500

gaccccagcc gtatccccgt ggacctccgg aggcacggtg cctgtgtctg 550

ggcttgtgtg aacccccttca ccatgcagga ggaccgcagc atggtgagcg 600

tgccggtgtt cagccaggtt cctgtgcgcc gccgcctctg cccgccaccg 650

ccccgcacag ggccttgccg ccagcgcgca gtcatggaga ccatcgctgt 700

gggctgcacc tgcatcttct gaatcgacct ggcccagaag ccaggccagc 750

agcccgagac catcctcctt gcacctttgt gccaagaaag gcctatgaaa 800

agtaaacact gacttttgaa agcaaaaaaa 830

FIGURE 5

cacggatgag gaccgctatc cacagaagct ggccttcgcc gagtgcctgt 50

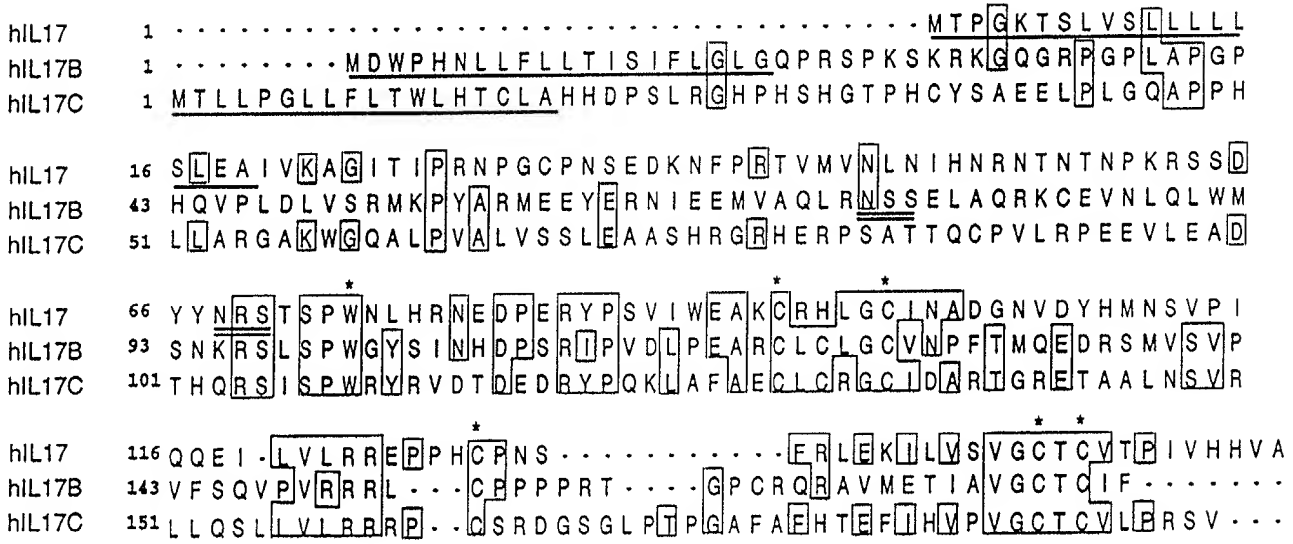
gcagaggctg tatcgatgca cggacgggcc gcgagacagc tgcgctcaac 100

tccgtgcggc tgctccagag cctgctggtg ctgcgccgcc ggccctgctc 150

ccgcgacggc tcggggctcc ccacacctgg ggcctttgcc ttccacaccg 200

agttcatcca cgtccccgtc ggctgcacct 230

FIGURE 6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hIL17B 1 ·····MDWPHNLLFLLTISIFLGLGQPRSPKSKRKGQGRPGPLAPGP
hIL17C 1 MTLLPGLLFLTWLHTCLAHHDPSLRGHPHSHGTPHCYSAEELPLGQAPPH
hIL17 16 SLEAIVKAGITIPRNPGCPNSEDKNFPRTVMVNLNIHNRNTNTNPKRSSD
hIL17B 43 HQVPLDLVSRMKPYARMEEYERNIEEMVAQLRNSSELAQRKCEVNLQLWM
hIL17C 51 LLARGAKWGQALPVALVSSLEAASHRGRHERPSATTQCPVLRPEEVLEAD
hIL17 66 YYNRSTSPWNLHRNEDPERYPSVIWEAKCRHLGCINADGNVDYHMNSVPI
hIL17B 93 SNKRSLSPWGYSINHDPSRIPVDLPEARCLCLGCVNPFTMQEDRSMVSVP
hIL17C 101 THQRSISPWRYRVDTDEDRYPQKLAFAECLCRGCIDARTGRETAALNSVR
hIL17 116 QQEI·LVLRREPPHCPNS·····FRLEKILVSVGCTCVTPIVHHVA
hIL17B 143 VFSQVPVRRRL···CPPPPRT····GPCRQRAVMETIAVGCTCIF·····
hIL17C 151 LLQSLIVIRRRP··CSRDGSGLPTPGAFAEHTEFIHVPVGCTCVLPRSV···

FIGURE 7A

Tue Apr 27 16:58:30 1999
/home/ruby/va/Molbio/carpenda/temp/aa.out

```
59294     1 MDWPHNLLFLLTISIFLGLGQPRSPKSKRKGQGRPGPLAPGP---HQVPL
62377     1 MTLLPGLLFLTWLHTCLAHHDP-SLRGHPHSHGTPHCYSAEELPLGQAPP

59294    48 DLVSRMKPYARM--EEYERNIEEMVAQLRNSSELAQRKCEV----NLQLW
62377    50 HLLARGAKWGQALPVALVSSLEAASHRGRHERPSATTQCPVLRPEEVLEA

59294    92 MSNKRSLSPWGYSINHDPSRIPVDLPEARCLCLGCVNPFTMQEDRSMVSV
62377   100 DTHQRSISPWRYRVDTDEDRYPQKLAFAECLCRGCIDARTGRETAALNSV

59294   142 PVF-SQVPVRRRLCPPP----PRTGPCRQRAVMETIAVGCTCIF
62377   150 RLLQSLLVLRRRPCSRDGSGLPTPGAFAFHTEFIHVPVGCTCVLPRSV
```

FIGURE 7B

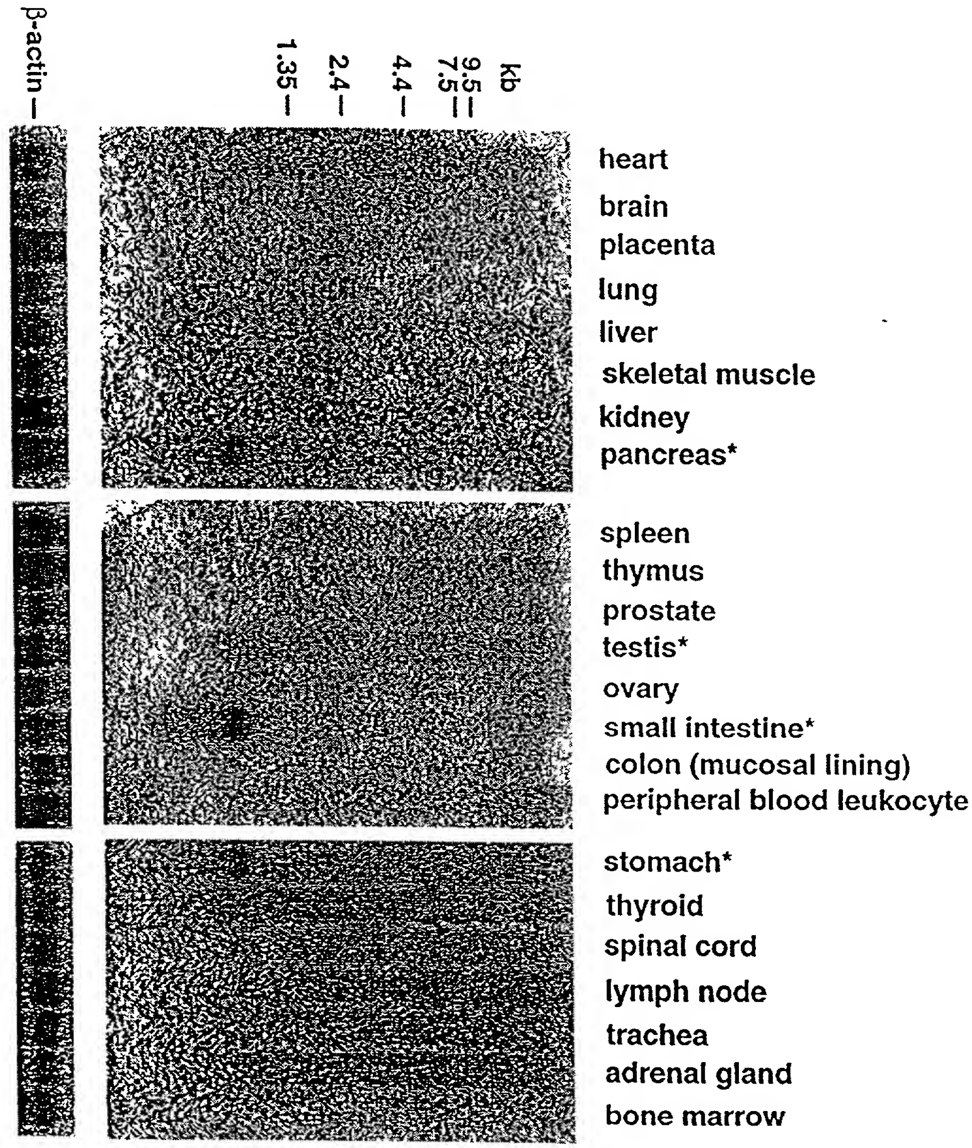


FIGURE 8

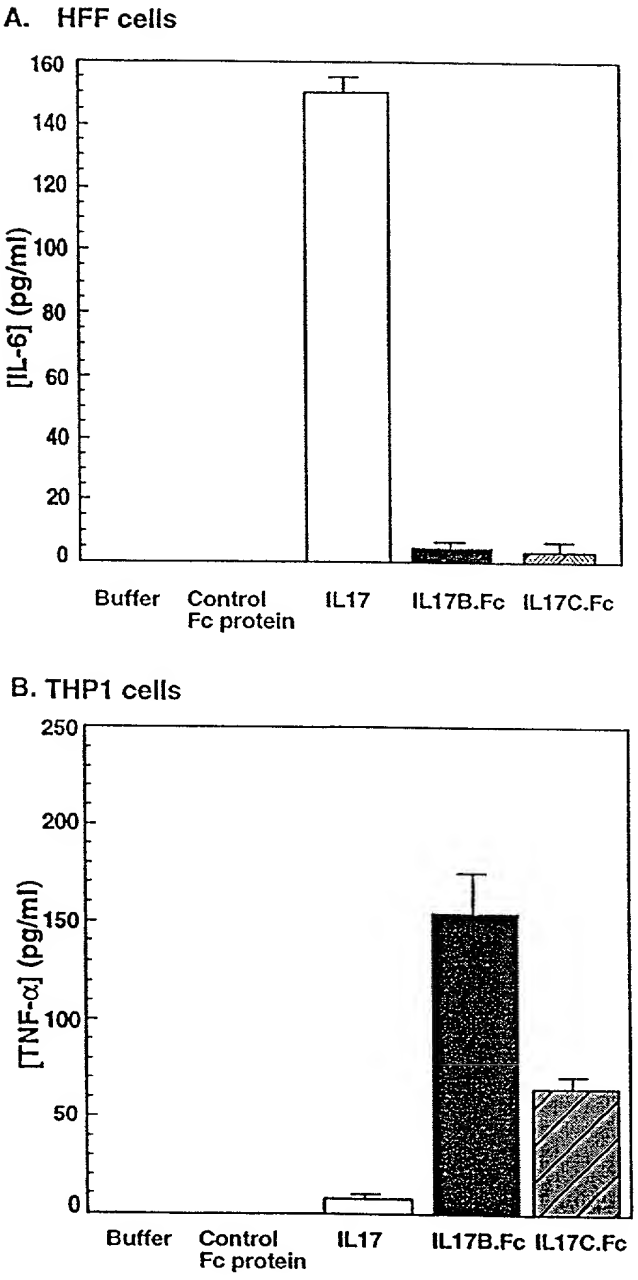
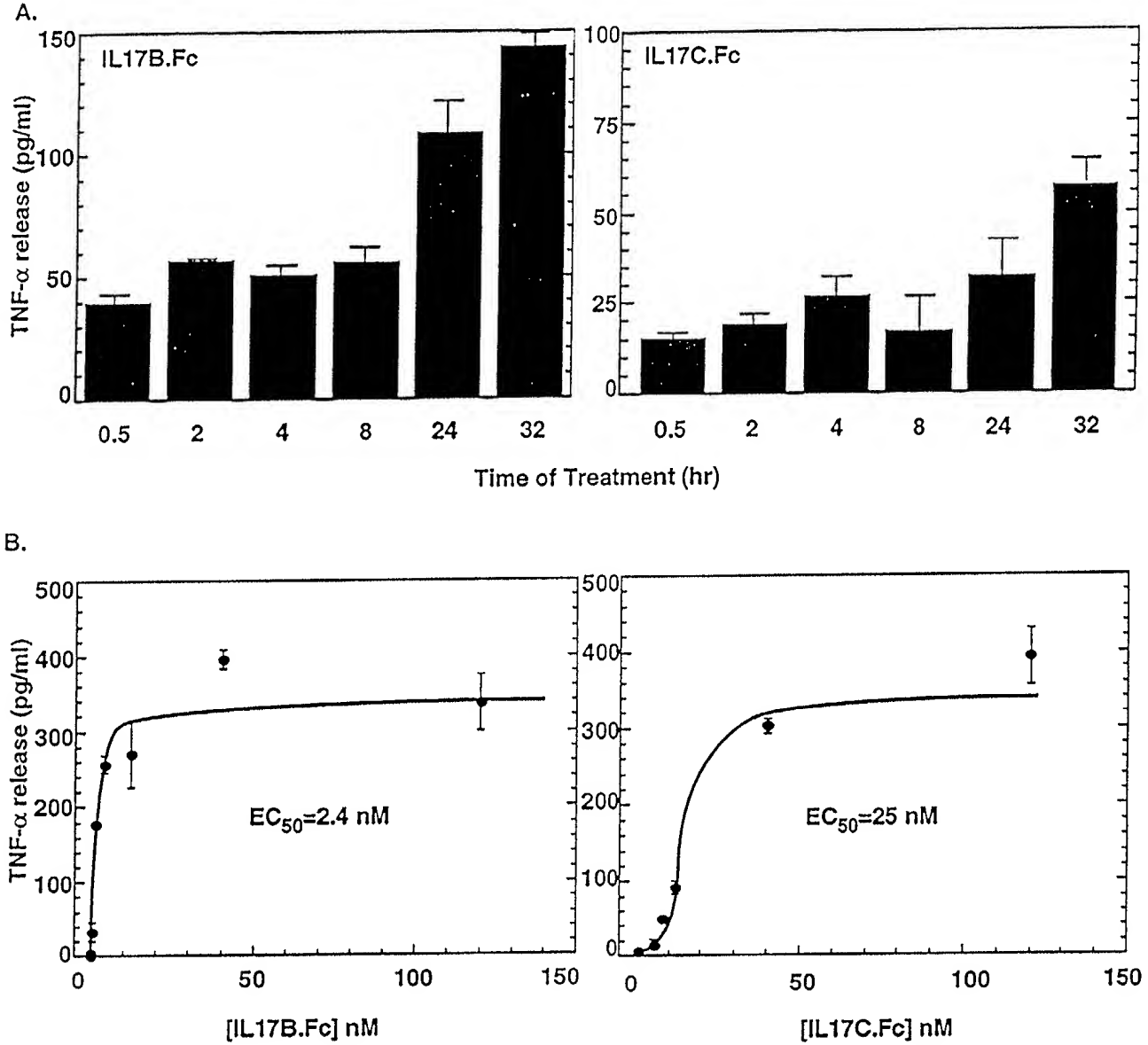

A. HFF cells
[IL-6] (pg/ml)
160
140
120
100
80
60
40
20
0
Buffer
Control Fc protein
IL17
IL17B.Fc
IL17C.Fc
B. THP1 cells
[TNF-α] (pg/ml)
250
200
150
100
50
0
Buffer
Control Fc protein
IL17
IL17B.Fc
IL17C.Fc

FIGURE 9

FIGURE 10



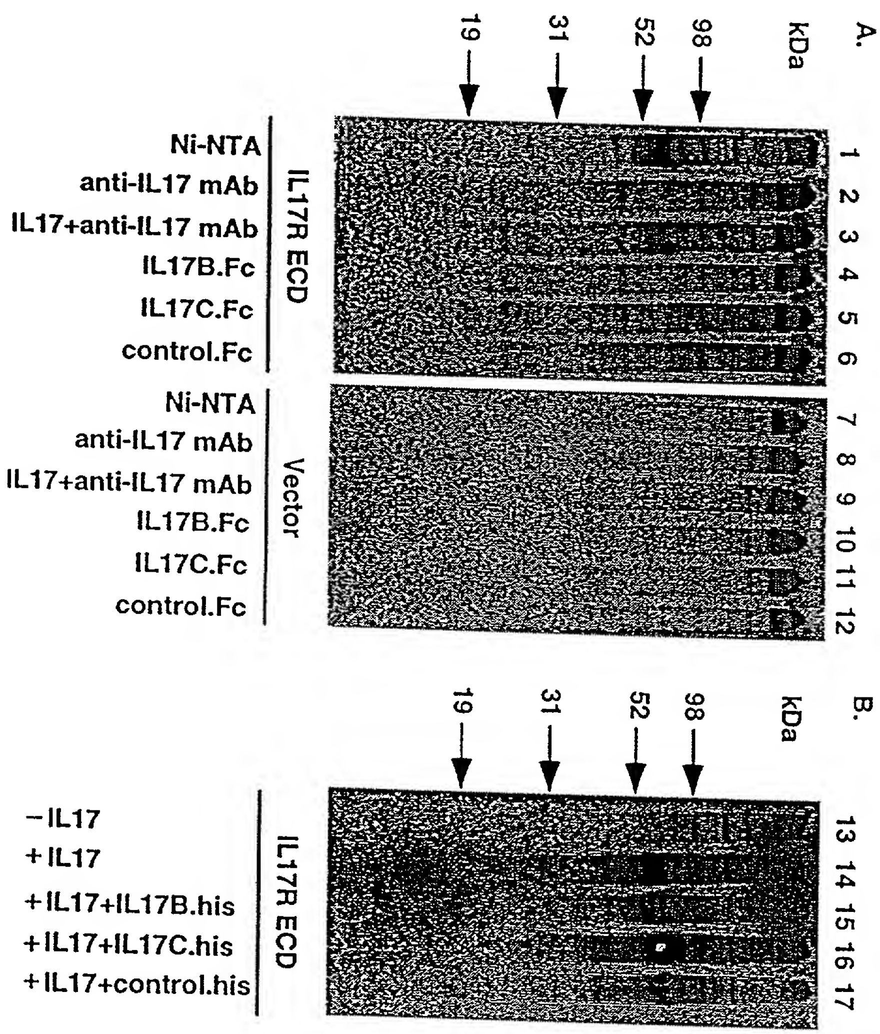

A.
kDa
98
52
31
19
1 2 3 4 5 6 7 8 9 10 11 12
IL17R ECD
Ni-NTA
anti-IL17 mAb
IL17+anti-IL17 mAb
IL17B.Fc
IL17C.Fc
control.Fc
Vector
Ni-NTA
anti-IL17 mAb
IL17+anti-IL17 mAb
IL17B.Fc
IL17C.Fc
control.Fc
B.
kDa
98
52
31
19
13 14 15 16 17
IL17R ECD
−IL17
+IL17
+IL17+IL17B.his
+IL17+IL17C.his
+IL17+control.his

FIGURE 11

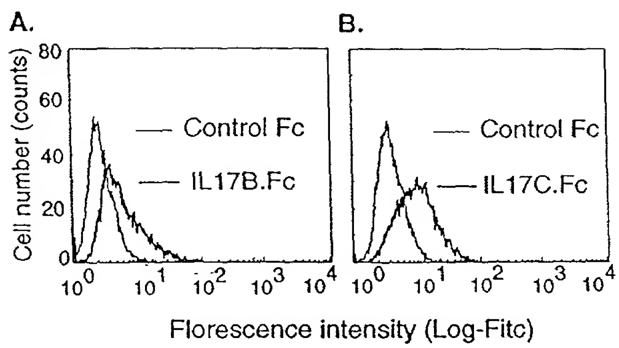

A.
B.
Cell number (counts)
80
60
40
20
0
Control Fc
IL17B.Fc
Control Fc
IL17C.Fc
10^0 10^1 10^2 10^3 10^4
10^0 10^1 10^2 10^3 10^4
Florescence intensity (Log-Fitc)

FIGURE 12

IL-17 induces breakdown and inhibits synthesis of cartilage matrix

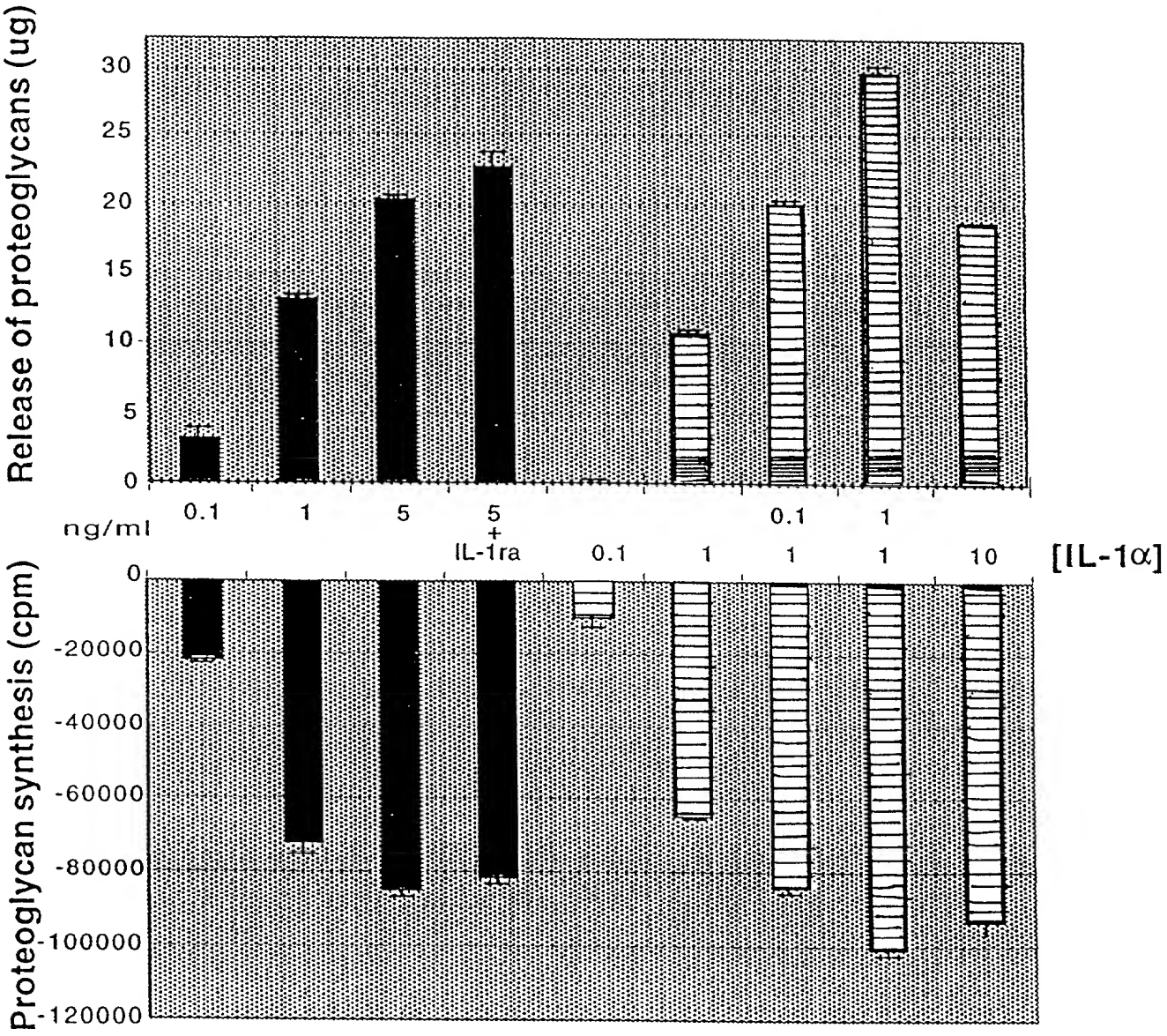


FIGURE 13

IL 17 increases basal and IL-1α-induced nitric oxide release

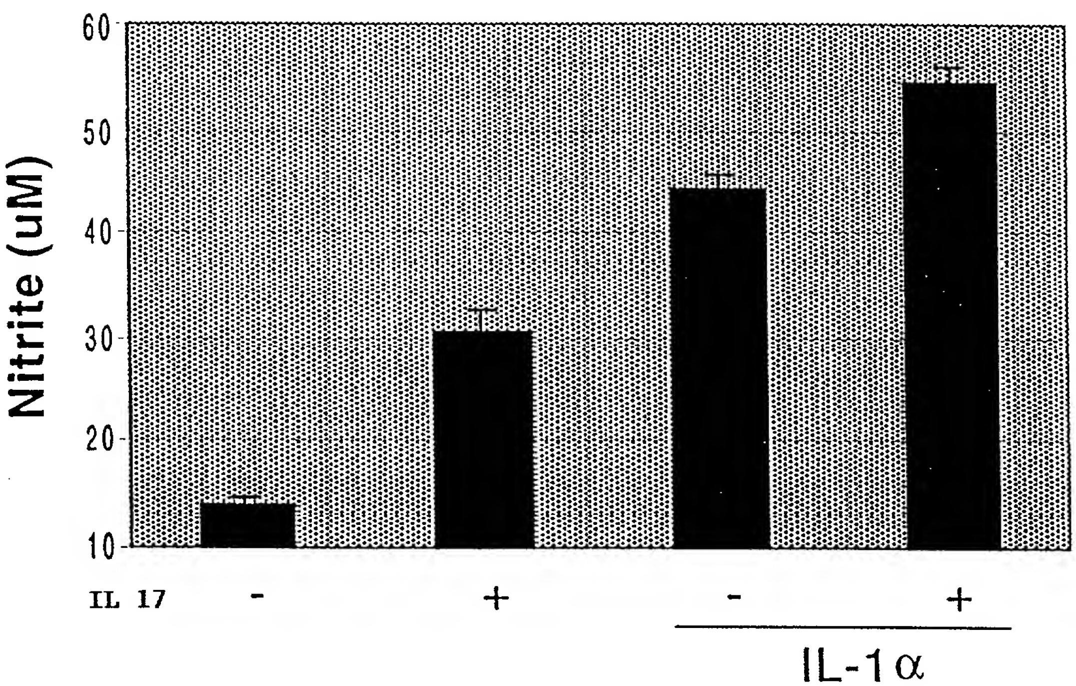


FIGURE 14

Inhibition of nitric oxide release does not block the detrimental effects of IL 17 on matrix breakdown or synthesis

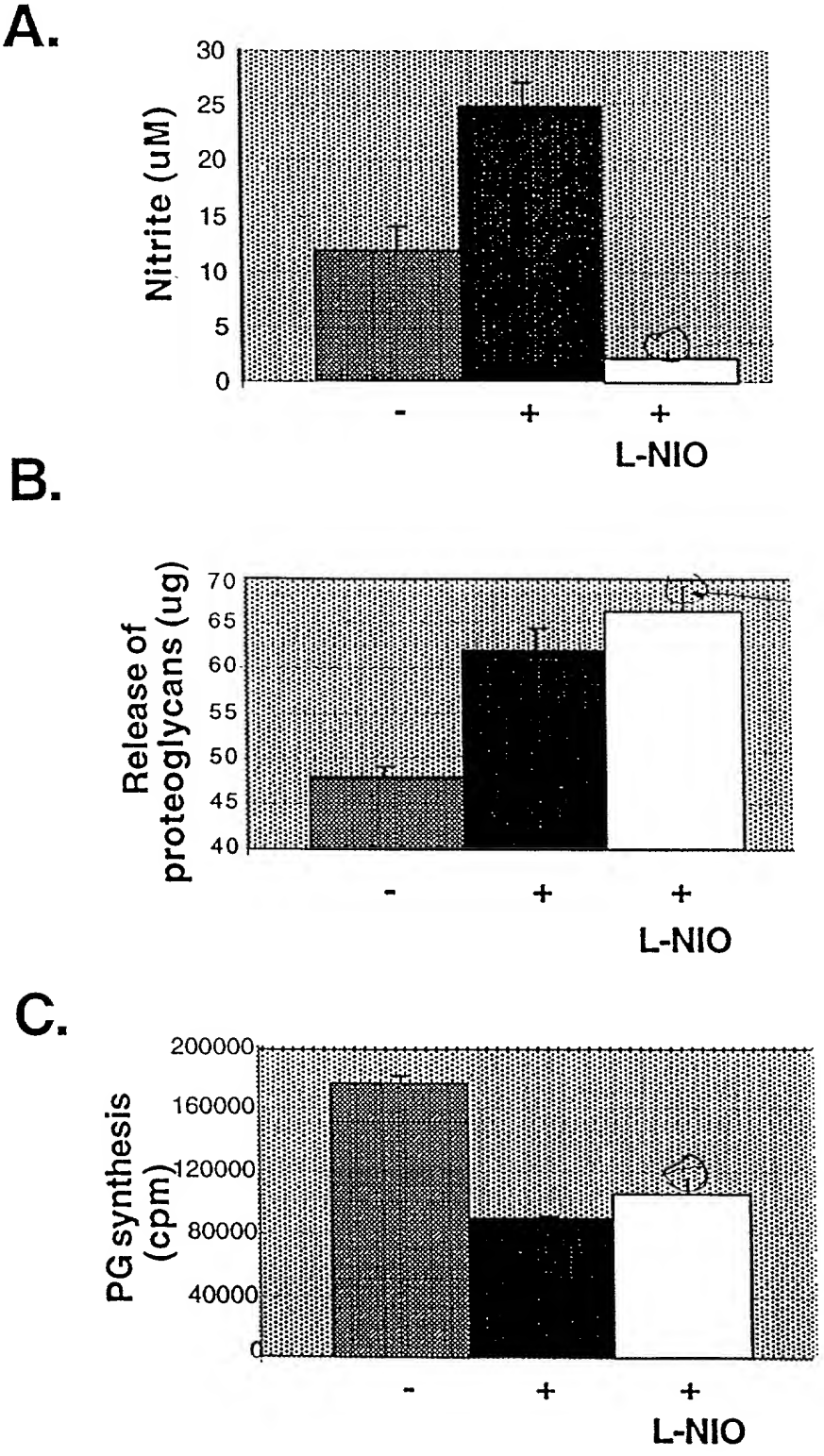


FIGURE 15

INHIBITION of NO release enhances IL1-α-induced matrix breakdown but not matrix synthesis

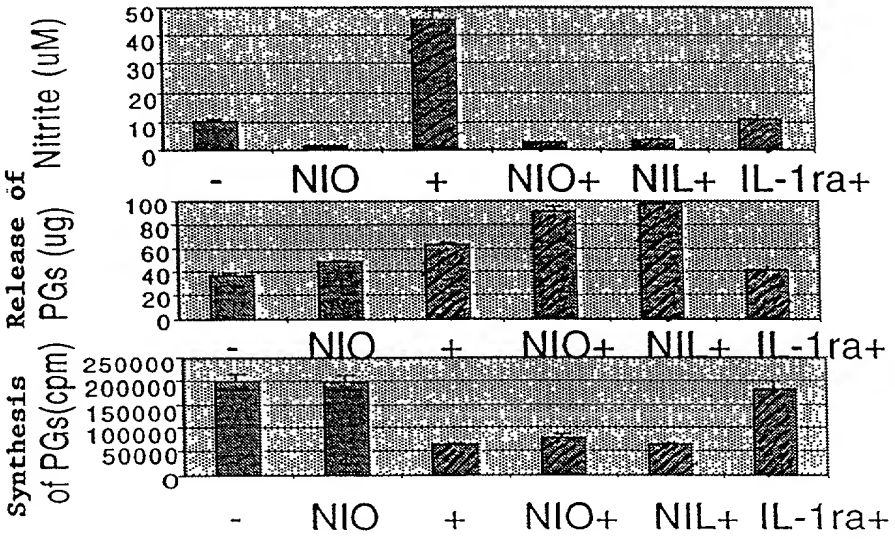


FIGURE 16

IL 17 homologue 1 (UNQ516) has positive effects on articular cartilage

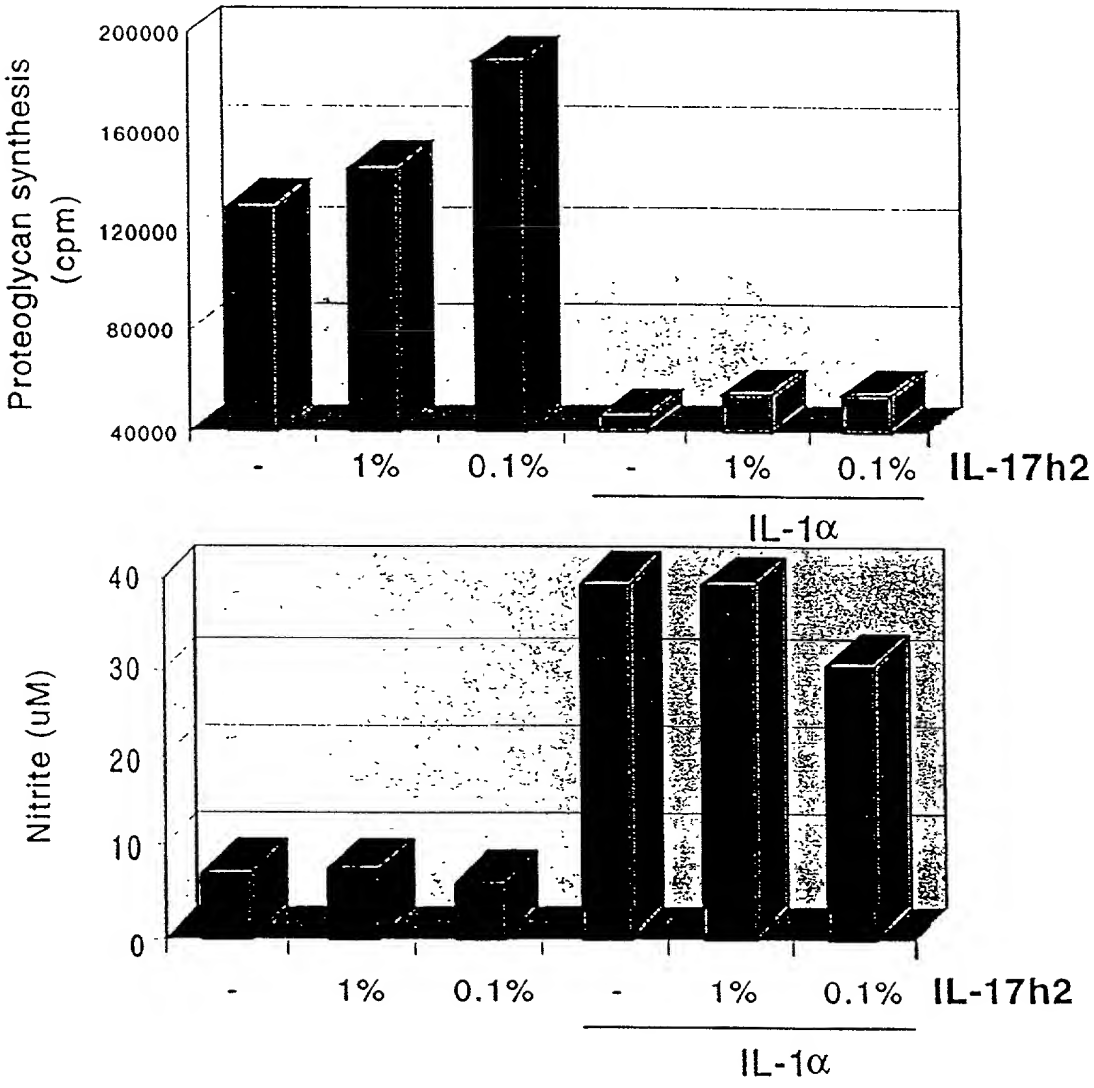


FIGURE 17

IL 17 homologue (UNQ 561) has detrimental effects on articular cartilage

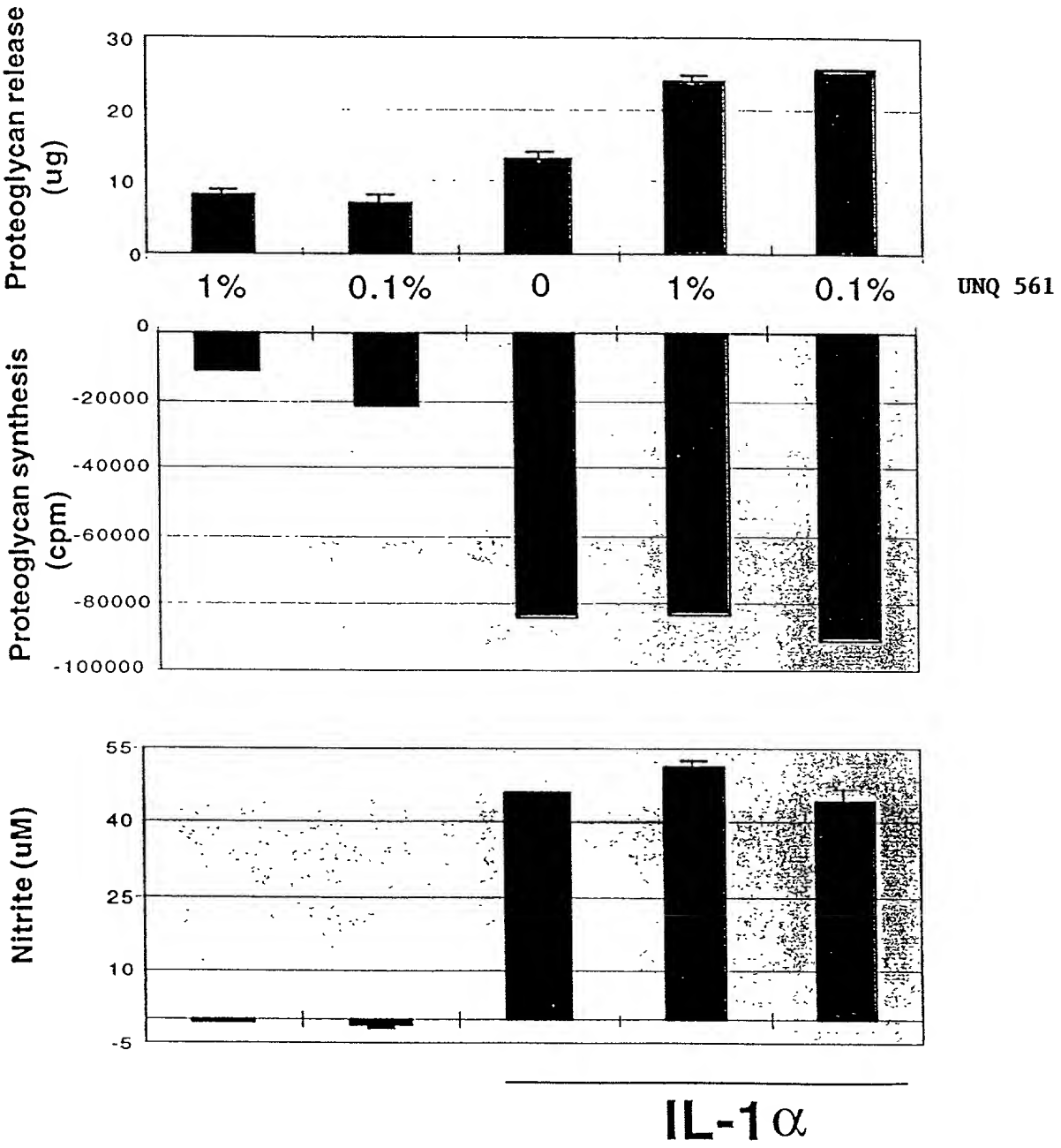


FIGURE 18